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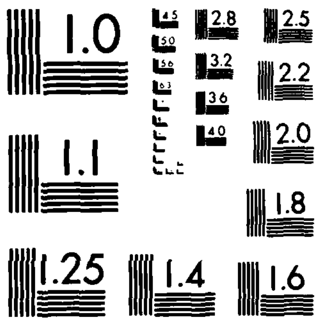

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A VALIDATED METHODOLOGY FOR DETERMINATION OF LABORATORY INSTRUMENT COMPUTER INTERFACE EFFICACY

ARTHUR D. LITTLE, INC.
Acorn Park
Cambridge, Massachusetts 02140

December 10, 1984

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Final report for period 12/15/83-12/05/84

Prepared for

TRIMIS PROGRAM OFFICE
5401 Westbard Avenue
Bethesda, Maryland 20816

The views, opinions, and findings contained in this report are those of the author(s) and should not be construed as an official Department of Defense position, policy, or decision, unless so designated by other official documentation.

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This report is intended to provide a methodology for determining when, and for which instruments, direct interfacing of laboratory instrument and laboratory computers is beneficial. This methodology has been developed to assist the Tri-Service Medical Information Systems ~~(TRIMIS)~~ Program Office ~~(TPO)~~ in making future decisions regarding laboratory instrument interfaces.

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SUMMARY

The methodology contained in the previous report, Proposed Methodology for Determination of Laboratory Instrument Computer Interface Efficacy, has been validated at two Department of Defense Medical Treatment Facilities (MTFs). The simplified benefits model can be expressed as follows:

Annual Time Savings = DNn,

where: D = time required to manually enter each data point (individual test result);

N = the average number of data points per instrument run;

n = the average number of daily runs,

and is sufficient to determine the efficacy of interfacing certain instruments to a laboratory system. This model applies to continuous mode instruments as well as those discrete mode instruments which do not require technician involvement.

For discrete mode instruments which do require technician involvement (or if system response time is poor), the proposed model is:

Annual Time Savings = [N(B-D)]n,

where: B = time required to ensure correct sequencing and matching of data.

We have calculated the time savings required to reach a break-even point for a range of instrument interface prices and corresponding average annual costs. The break-even analyses used empirical data to estimate the number of data points run per day that are required to meet the break-even point. The results indicate, for example, that at a purchase price of $3,000, an instrument interface will be cost-effective if the instrument is utilized for at least 154 data points per day if operated in the continuous mode, or 216 points per day if operated in the discrete mode.

Although this model can help to ensure that instrument interfaces are cost effective, additional information should be considered in making the interface decisions. A reduction in results transcription errors may be a major benefit of instrument interfacing. Due to the difficulty and cost of measurement, this factor has not been

quantified in this validation effort. However, reduction of transcription errors was mentioned in all interviews with laboratory personnel.

Finally, technicians' attitudes toward automation affects the use of interfaced instruments. We observed cases of interfaced instruments being run in the manual mode, due primarily to negative technician attitudes towards automation.

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I. INTRODUCTION

Automated laboratory instrument interfaces allow test result data to be entered directly from a lab instrument (with an electronic output) to a computer. This can be advantageous for an instrument which has a large number of numerical results per run, by saving technician time required to manually input data into the computer.

This report is intended to provide a methodology for determining when, and for which instruments, direct interfacing of laboratory instruments and laboratory computers is beneficial. This methodology has been developed to assist the Tri-Service Medical Information Systems (TRIMIS) Program Office (TPO) in making future decisions regarding laboratory instrument interfaces.

Section II describes the differences in operations between on-line and manual input systems. Section III discusses the potential costs and benefits associated with direct interfacing. Sections IV and V discuss two models for analyzing benefits: a complete theoretical model and a simplified version based on preliminary estimates of the parameters. Section VI presents the results of our validation study.

II. OPERATION OF LABORATORY INSTRUMENTS UNDER MANUAL AND ON-LINE CONDITIONS

A. MANUAL ENTERING OF RESULTS

Manual entering of laboratory results typically proceeds as follows:

- The technician obtains test results from the laboratory instrument.
- The technician manually writes the results on a form.
- The technician transports the results to the computer terminal.
- The technician sets up the computer for entering results manually, and enters each result via the terminal keyboard.

B. ON-LINE MODE

In the on-line mode of operation, the following steps are taken by the technician:

- First, the computer must be set up to receive data from the laboratory instrument. This involves entering a few instructions via a laboratory computer terminal indicating which instrument will be run in the interfaced mode. For instruments that are normally run in the interfaced mode (e.g., the SMAC), the technician will generally know the instructions. For instruments that are infrequently used in the on-line mode, the instructions may have to be looked up.
- The run is carried out automatically on the laboratory instrument, with results entering the computer automatically.
- After the run is completed, the technician must verify that the results have been entered correctly into the computer. This includes: 1) ensuring that "matching" between specimen sequence number and patient access number is correct; and 2) that results have been entered correctly.

- Finally, in the on-line mode, the technician reviews the results via the terminal to ensure that the sequence of specimens, controls, and blanks have been entered correctly, since a mistake in sequencing cannot be detected by the computer.

Thus, the manual and on-line modes differ in several ways. First, the set-up time for the on-line mode is probably longer. Second, the time required to enter results in the manual mode is eliminated in the on-line mode. Third, additional time may be required in the on-line mode to ensure the proper sequencing of results entry. Finally, the manual mode may be more flexible; that is, it may be more convenient for the technician to alter sample sequencing (i.e., to rerun samples or standards).

In practice, high volume instruments (those with a large number of data points per run) such as the SMAC and Coulter Counter machines tend to be run in the interfaced mode, while low volume instruments tend to be run in the manual mode. Medium volume instruments may be run in the on-line mode for some runs (such as large batches of routine samples in the a.m.) and in the manual mode for other runs (smaller p.m. runs). Choice of operating mode depends on whether the time required to set up for an on-line run offsets the time savings from on-line data collection.

III. POTENTIAL COSTS AND BENEFITS

The costs associated with instrument interface include one-time procurement costs and recurring maintenance costs. The initial cost of procuring interface capability includes the cost of hardware (e.g., cables, "black boxes," A/D converters, etc.) and the cost of any software modifications to existing laboratory computer software. The ongoing costs are related mainly to software maintenance and, possibly, to hardware maintenance.

One benefit associated with on-line instrumentation interfacing may be savings in technician time. These savings could accrue from: elimination of manual results entry, elimination of calculations required to obtain results, and elimination of set-up time for manual results entry. Some or all of these time savings may be offset by the time required to set up for an interfaced run and the increased time required for verification. The difference between technician time required to complete an instrument run in the manual mode versus the automated mode must be determined in order to analyze the potential benefits of on-line instrument interfaces. The proposed methodology for determining this difference is described in the next section.

IV. MODEL

We have developed a theoretical model to determine the potential benefits of interfacing a laboratory instrument to a laboratory system.

We assume that the time cost of producing a run with N data points (data points = number of samples x tests per sample) in the automated (on-line) mode is:

$$T_1 = A + BN,$$

where A is the "setup" time for the run, and includes the following:

A_1 = initiating the run on the computer

A_2 = stopping the run

A_3 = filing.

That is, $A = A_1 + A_2 + A_3$.

B is the time cost per test, including:

B_1 = time to ensure correct sequencing

B_2 = time to ensure correct "matching."

Thus $B = B_1 + B_2$.

If the run is performed in the manual mode, the time involved is assumed to be:

$$T_2 = C + DN,$$

where C is the setup time to enter the results manually and D is the time to enter each test result.

We anticipate that the times for producing runs will be as follows:

For any individual instrument run, it is more efficient to use the manual mode if the run produces less than the N_B data points. Conversely, the on-line mode is more efficient for runs with greater than N_B data points.

To determine annual savings for a particular instrument, T_1 and T_2 must be determined. In addition, two annual average quantities must be known:

1) N = average number of data points per major routine daily run.
2) n = average number of major routine daily runs.

These averages should be based on major routine runs in order to exclude small runs of STAT samples and repeat samples, which would skew the pertinent averages.

The annual time savings (ATS) can be computed using the following calculations:

$$ATS = [[(A_1 + A_2 + A_3) + (B_1 + B_2) N] - (C + DN] n$$

$$= [(A + BN) - (C + DN)] n$$

$$= (T_1 - T_2) n.$$

To obtain the annual benefit in dollars, the annual time savings must be multiplied by the average cost of a technician.

Annual Time Savings x Average Cost of Technician = Annual Benefit.

Each on-line interface can be cost-justified if the Average Annual Benefit - Annual Cost is positive.

This model does not take into account potential benefits that are difficult or impossible to value, such a decrease in transcription errors. The model estimates the time savings generated by an on-line interface for a particular instrument. The time savings per run from the interface are multiplied by the average number of runs per year to give the annual time savings from the interface. These time savings can then be balanced against the amortized one-time costs and the recurring costs to provide a basis for deciding whether an interface is justified. The time savings per run (T_1-T_2) can be generally applied to all instruments of a particular type (e.g., SMAC).

To determine the time savings, the model indicates that certain parameters must be determined for each type of instrument considered for interfacing:

A_1 = times put in initiating the run in the on-line mode

A_2 = times put in stopping the run in the on-line mode

A_3 = times put in filing the results in the computer files

B_1 = verification time to insure correct sequencing in the on-line mode

B_2 = verification time to insure correct matching in the on-line mode

C = set-up time in the manual mode

D = result entry time in the manual mode.

These parameters can be determined by on-site time-motion studies. The parameters would have to be determined for each type of potential interface instrument at least at one site, and preferably at more than one site.

V. SIMPLIFIED MODEL

Based on interviews with technicians and observations of interfaced and non-interfaced laboratory instruments during a site visit to Malcolm Grow USAF Medical Center, Andrews Air Force Base, the above theoretical methodology can be simplified.

On-line instrument runs can be divided into two categories: runs produced on "continuous" machines; and runs produced on "discrete" machines. Continuous machines are those instruments that allow all of the data from a complete run to be entered automatically into the computer system. An example of a continuous machine is the HYCEL 8700. Discrete machines are those instruments that produce results one sample at a time, such as the Coulter S+. For continuous instruments, a run with many data points is set up and initiated at one time, the data is automatically entered for the entire run, and the technician simply merges the data file into the appropriate worksheet in the laboratory system and spot checks the data for correct matching. In contrast, discrete machines run one sample at a time. The technician must set up a separate worksheet for each sample. Thus, the results are entered automatically only on a sample-by-sample basis.

For continuous instruments, quantities A and C in the model are very small since the set-up time can be averaged across a large number of data points. Quantity B is trivial in terms of time per data point, since a continuous mode instrument can include as many as 3,000 data points per run. For example, the average time required for sequencing (B_1) and matching (B_2) in the HYCEL example is about five minutes per run. Thus, B_1+B_2 is about 0.1 second/data point and can be dropped from the formula due to insignificance.

The time savings formula for continuous mode instruments becomes:

Annual Time Savings (ATS) = DNn.

In the discrete mode, the set-up time for each sample is an important factor. Since a separate worksheet must be called for each sample, the amount of time required for set up depends directly on the

system response time. In the Malcolm Grow laboratory, this time varied from two seconds to thirty seconds. However, since the set-up time (essentially the time required to call up each worksheet) is the same for both the automated and manual modes, both A and C can drop out of the on-line and manual models, respectively.

Thus, the formula for ATS for discrete mode instruments becomes:

$$\begin{aligned} ATS &= (BN-DN)n \\ &= [N(B-D)]n. \end{aligned}$$

In this case, the parameters to be measured for the continuous instruments are:

D, the time required to manually enter each data point;

N, the average number of data points per daily run;

n, the average number of daily runs.

In the discrete mode, an additional parameter to be measured is B, the time required to ensure correct sequencing and matching of actual test results with those entered in the system.

From the visit to Malcolm Grow, rough estimates of time requirements related to the ATS formulae were made. In general, the time required to enter one data point (D) is about 10 seconds for both the continuous and discrete modes. The time required for sequencing and matching (B) in the discrete mode is approximately 15-20 seconds per sample, or 2 seconds per data point.

The volume of data points required per instrument to cost-justify an automated interface can be calculated for the hypothetical case stated previously. A daily time savings (TS) of 18 minutes, or 1,080 seconds, would be the break-even point.

For the discrete mode, assuming one major run per day:

$$\begin{aligned} \text{Daily TS} &= (B-D)N \\ &= (2-10)N = -8N \text{ sec.} \end{aligned}$$

The break-even number of data points per day N_B, is

$$N_B = \frac{1080 \text{ seconds}}{8 \text{ seconds}} = 135.$$

For the continuous mode:

$$\text{Daily TS} = DN = 10N \text{ sec.}$$

$$N_B = \frac{1080}{10} = 108$$

Thus, for our example, an average of 135 data points per day in the discrete mode and 108 data points in the continuous mode would cost-justify an automated interface.

VI. VALIDATION

To validate the instrument interface methodology, we collected data at two DoD medical treatment facilities. The results of these visits are outlined below.

A. METHODOLOGY

A two-day visit was made to each of two sites that use the Tri-Service Laboratory (TRILAB) system: Naval Hospital, San Diego, and Malcolm Grow USAF Medical Center, Andrews Air Force Base. The instrument interface utilization survey forms, which are contained in Appendix A, were used during the visits. In addition, timed observations were made of various coefficients used in the laboratory instrument computer interface efficacy model. These observations focused primarily on the amount of time required to manually enter data into the TRILAB system.

B. INSTRUMENT INTERFACE UTILIZATION

Table 1 provides information from the instrument interface utilization surveys at Naval Hospital, San Diego, and Malcolm Grow USAF Medical Center. Naval Hospital, San Diego, has six instruments interfaced to the TRILAB system: three in the chemistry lab and three in Hematology. With the exception of the backup Coulter counter, all the instruments are used daily and, assuming the TRILAB system is operating, always in the interfaced mode. The Astra-8 and Astra-4 machines are generally used for STAT specimens. However, if the SMAC-II is not operating, the Astra instruments perform routine tests. In Hematology, the Hematrac and Coulter S+ are used routinely in the interfaced mode.

Malcolm Grow currently has two instruments operating in the interfaced mode: the HYCEL-8700 and the Coulter S+. In addition, a DuPont ACA autoanalyzer has an interface but is not used in the interfaced mode. This seems to be due to mechanical problems with the interface itself.

The original decision of which instruments to interface to the TRILAB system was generally made by a "seat of the pants" method. That is, the facilities were asked which instruments should be

TABLE 1

INSTRUMENT INTERFACE UTILIZATION AT
MALCOLM GROW USAF MEDICAL CENTER AND
NAVAL HOSPITAL, SAN DIEGO

Site	Instrument	STAT or Routine	% of On-Line Data Entry
Malcolm Grow	HYCEL 8700	Routine	100
USAF Med Cen.	Coulter S+	Routine	90
	ACA	STAT	0
	ARIA II (a)	Routine	0
	ARIA II (b)	Routine	0
NAVHOSP,	Astra-8	Both	100
San Diego	Astra-4	Both	100
	SMAC-II	Routine	100
	Coulter S+ (a)	Routine	100
	Coulter S+ (b)	STAT/Backup	0
	Hematrac	Routine	100

interfaced, and the response tended to be the high-volume instruments. For example, approximately 80 percent of all chemistry lab tests are performed on three instruments at Naval Hospital, San Diego: SMAC-II, Astra-4, and Astra-8. Malcolm Grow originally requested interfaces for the HYCEL, the Coulter S+, the ACA, and two ARIA II (automated RIA) machines. The decision was based on the volume of tests performed on the machines and the ability of the machines to be interfaced. The ARIA machines and the ACA machines have not been used successfully in an interface mode. The reasons for the not using interface for these machines is not entirely clear. However, the attitudes of the technicians assigned to the machines seemed to be a factor.

While Naval Hospital, San Diego, seems to effectively utilize the interfaces and does not seem to need additional interfaces, Malcolm Grow would like to add interfaces to at least two new instruments. Again, it appears that the decision to add interfaces is based more on the ability of the new instruments to be interfaced rather than any analysis of volume, costs, or benefits.

The factors that were considered to be important in determining the actual utilization of interfaces included:

- Decreased transcription errors;
- Increased speed of data entry;
- Time savings;
- User friendliness; and
- Lack of mechanical problems with the interface.

C. RESULTS

Table 2 presents the average measured time to enter data points manually to the TRILAB system, and to match and file results.

Matching and filing times were not recorded for the Coulter S+ since the filing took place while the technician was preparing the next sample. The technicians in the Hematology Lab at Naval Hospital, San Diego, noted that when first installed, the computer often had such a slow response time that they had to wait between samples. However, this problem seems to have been solved. In general, the

TABLE 2

AVERAGE TIME FOR DATA ENTRY
MALCOLM GROW USAF MEDICAL CENTER AND NAVAL HOSPITAL, SAN DIEGO

	Malcolm Grow USAF Med Center			NAVHOSP San Diego			Total		
	No. of Points	Average Time (sec.)	Standard Deviation (of mean)*	No. of Points	Average Time (sec.)	Standard Deviation (of mean)*	No. of Points	Average Time (sec.)	Standard Deviation (of mean)*
Manual Data Entry	204	7.14	0.69	159	6.79	0.33	363	6.99	0.41
Matching and Filing (continuous instruments)	3	3.04	0.79	4	3.60	1.58	7	3.4	1.33
Set Up Computer	3	3.20	2.18	3	2.50	1.38	6	2.5	1.75

*See Appendix B for description of methodology used in calculating Standard Deviation.

matching and filing activities on the discrete (Coulter) instruments are insignificant since the technician has to wait while the machine analyzes each sample.

The time required to set up the computer varied somewhat according to the instrument, technician, and length of run involved. However, the assumption that the coefficients A, B and C are insignificant for large runs on continuous instruments is supported by our observations. For example, the average time required for matching and filing for the SMAC instrument at Naval Hospital, San Diego, was about 3 minutes. The typical run length was 60 samples x 20 tests = 1,200 test results. Thus, the average time for B on the SMAC was 0.15 seconds. The simplified formula,

$$ATS = DNn$$

holds true for continuous mode instruments (assuming relatively large runs).

The major alteration in the simplified interface methodology is the exclusion of B from the discrete mode instrument formula in most cases. As long as the system response time is short enough to allow sample preparation, filing, and setup while the instrument is processing a sample, the B term can be dropped. In these cases, B will be absorbed by otherwise non-productive technician time. However, in the case of discrete instruments that require active technician involvement during sample processing (such as the Hematrac), B must be included in the time savings calculation. Thus, the formula for calculating interface time savings for discrete mode instruments becomes

$$ATS = DNn$$

for instruments that require technician waiting during sample processing (assuming adequate system response time), and remains

$$ATS = [N(B-D)]n$$

for instruments that require active technician involvement in sample processing.

D. COST CALCULATIONS

The purchase price of an interface is estimated to be in the range of $3,000-$10,000. The average annual costs of interfaces are calculated in Table 3. These costs are as follows:

Purchase Price ($)	Average Annual Cost ($)
$ 3,000	$ 877
5,000	1,461
7,000	2,045
10,000	2,922

These calculations were obtained assuming: (1) a five-year lifetime for the interface; (2) a discount rate of 10%; (3) an inflation rate of 5%; and (4) an annual maintenance cost of 12% of the purchase price.

E. BENEFIT CALCULATIONS

The observed value of 7 seconds per data point for manual entry of data alters the calculation of a break-even point (labor-savings ÷ interface cost) for instrument interfaces. Using the annual costs derived in Section D, the average daily volume of data points required per instrument to break even can be estimated.

Table 4 contains the calculations of daily technician time savings required to break even for the range of purchase prices in Section D. Table 5 presents the calculation of the minimum average daily run size (in data points) required to reach the break-even point. The results indicate, for example, that at a purchase price of $3,000, an instrument interface will be cost-effective if the instrument is utilized for at least 154 data points per day if operated in the continuous mode, or 216 points per day if operated in the discrete mode.

TABLE 3

INSTRUMENT INTERFACE COST CALCULATIONS

COST CALCULATIONS

INTEREST= 5
DISCOUNT= 10
INTERFACE COST= 5000

YEAR	1	2	3	4	5
PURCHASE	1000.00	1050.00	1102.50	1157.63	1215.51
MAINTENANCE	600.00	630.00	661.50	694.58	729.30
TOTALS	1600.00	1680.00	1764.00	1852.20	1944.81
DISCOUNTED	1600.00	1527.27	1457.85	1391.59	1328.33
TOTAL	7305.04				
YEARLY EXPENSE	1461.01				

INTEREST= 5
DISCOUNT= 10
INTERFACE COST= 7000

YEAR	1	2	3	4	5
PURCHASE	1400.00	1470.00	1543.50	1620.68	1701.71
MAINTENANCE	840.00	882.00	926.10	972.41	1021.03
TOTALS	2240.00	2352.00	2469.60	2593.08	2722.73
DISCOUNTED	2240.00	2138.18	2040.99	1948.22	1859.66
TOTAL	10227.06				
YEARLY EXPENSE	2045.41				

INTEREST= 5
DISCOUNT= 10
INTERFACE COST= 10000

YEAR	1	2	3	4	5
PURCHASE	2000.00	2100.00	2205.00	2315.25	2431.01
MAINTENANCE	1200.00	1260.00	1323.00	1389.15	1458.61
TOTALS	3200.00	3360.00	3528.00	3704.40	3889.62
DISCOUNTED	3200.00	3054.55	2915.70	2783.17	2656.66
TOTAL	14610.08				
YEARLY EXPENSE	2922.02				

INTEREST= 5
DISCOUNT= 10
INTERFACE COST= 3000

YEAR	1	2	3	4	5
PURCHASE	600.00	630.00	661.50	694.58	729.30
MAINTENANCE	360.00	378.00	396.90	416.75	437.[illegible]
TOTALS	960.00	1008.00	1058.40	1111.32	[illegible]
DISCOUNTED	960.00	916.3[illegible]	[illegible]	[illegible]	[illegible]
TOTAL	4383.02				
YEARLY EXPENSE	876.60				

TABLE 4

CALCULATION OF DAILY TIME SAVINGS REQUIRED TO BREAK EVEN

Purchase Price	Average Annual Cost	Required Time Savings* Annual (hours)	Daily (mins.)**
$ 3,000	$ 877	77	18
5,000	1,461	128	30
7,000	2,045	179	41
10,000	2,922	256	59

*Based on a technician cost of $11.40/hour.
**Based on 260 working days per year.

TABLE 5

CALCULATION OF AVERAGE DAILY RUN SIZE REQUIRED TO BREAK EVEN

Purchase Price	Break-even Daily Time Savings (sec.)*	Average Daily Data Points Required: Continuous**	Average Daily Data Points Required: Discrete***
$ 3,000	1,080	154	216
5,000	1,800	257	360
7,000	2,460	351	492
10,000	3,540	506	708

*From Table 4.
**Formula is N = TS/7.
***Formula is N = TS/5.

APPENDIX A

INSTRUMENT INTERFACE UTILIZATION SURVEY

APPENDIX A

I. INSTRUMENT INTERFACE UTILIZATION SURVEY

Instrument (Name, Model #)	Department (Chem, etc.)	STAT or Routine	Typical Monthly Volume		Interface Utilization			Estimate the % of on-line data entry
			Specimens	Average Tests/Specimen	Usually	Sometimes	Rarely	

II. Please describe how the decision to interface certain instruments in your lab was made. Who made the decision and what methodology (e.g., "seat-of-the-pants," test volume, type of output, etc.), if any, was utilized?

III. Do you have additional instruments that you believe should be interfaced? If so, why? Should any of the currently interfaced instruments not be interfaced? Why?

IV. Please list the factors you think are important in determining the actual use of on-line data entry for interfaced instruments.

APPENDIX B

CALCULATION OF STANDARD DEVIATIONS FOR ESTIMATED RATIOS

APPENDIX B

CALCULATION OF STANDARD DEVIATIONS FOR ESTIMATED RATIOS

The following technique was used to determine standard deviations of the timed observation data. This technique is used whenever a mean that is estimated from a simple random sample is the ratio of two variables, both of which vary from unit to unit. The estimated quantity or $\hat{R}$ is more complicated than that of x because both the numerator and the denominator vary from sample to sample.

If quantities y_i, x_i measured for each unit of a simple random sample of size n (assumed to be large), the variance of $\hat{R}$ is approximately

$$V(\hat{R}) = \frac{1}{n\bar{x}^2} \frac{\Sigma(y_i-\hat{R}x_i)^2}{n-1}$$

where $\hat{R}$ is the ratio of the population means.

In samples, $\hat{R}$ is usually a slightly biased estimate of R. However this bias becomes neglible in large samples. The bias of $\hat{R}$ is on the order of $\frac{1}{n}$.

The standard deviation of R is obtained by taking the square root of the variance.

$$s(\hat{R}) = \frac{1}{\sqrt{n}\,\bar{x}} \sqrt{\frac{\Sigma((y_i-\hat{R}x_i)^2}{n-1}}$$

In this formula, n is the number of samples, $\bar{x}$ is the average number of observations per sample, y_i is the numerator of the ratio (in the timed observation data y_i is the total time for an observation of several activities), x_i is the number of elements per sample, and R is the measured ratio of $\frac{\hat{y}}{\hat{x}}$.

Reference: Cochran, Sampling Techniques, 2nd ed., pp. 29-33, John Wiley and Sons, New York 1963.

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